L5 ANSWER 1 OF 24 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:545508 CAPLUS
DOCUMENT NUMBER: 135:132464
TITLE: Cyclic peptide inhibitors of VEGF, VEGF-C, and VEGF-D, preparation methods, pharmaceutical compositions, and therapeutic use
INVENTOR(S): Achen, Marc G.; Hughes, Richard A.; Stacker, Steven; Cendron, Angela
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001052875	A1	20010726	WO 2001-US1533	20010118

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-176293 P 20000118
US 2000-204590 P 20000516

AB The invention provides monomeric monocyclic peptide inhibitors and dimeric bicyclic peptide inhibitors based on exposed loop fragments of a growth factor protein, e.g. loop 1, loop 2 or loop 3 of VEGF-D, as well as methods of making them, pharmaceutical compns. contg. them, and therapeutic methods of use.

REFERENCE COUNT: 3
REFERENCE(S):
(1) Children's Medical Center Corporation; WO 99/29861 A1 1999 CAPLUS
(2) Jia; Biochem Biophys Res Comm 2001, V283, P164 CAPLUS
(3) Piossek; J Biol Chem 1999, V274(9), P5612 CAPLUS

L5 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:338762 CAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398 P 19991105
US 2000-196571 P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic ***damage*** at the tissue, organ or system level. Gene databases arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

L5 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:247374 CAPLUS
DOCUMENT NUMBER: 134:276523
TITLE: Hypoxia-related human genes and their encoded proteins and diagnostic and therapeutic uses
INVENTOR(S): Denko, Nicholas C.; Giaccia, Amato J.; Green, Christopher J.; Laderoute, Keith R.; Schindler, Cornelia; Koong, Albert Ching-Wei
PATENT ASSIGNEE(S): Varian Associates, Inc., USA
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001023426	A2	20010405	WO 2000-US27189	20001002

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,

CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 1999-410375 A 19990930
AB The polynucleotide and polypeptide sequences of two novel hypoxia-inducible human and murine genes, HIG1 and HIG2, are described. In addn., a no. of known genes and ESTs are established as being hypoxia-inducible and hypoxia-repressible. Polynucleotide and polypeptide arrays comprising the hypoxia-inducible and hypoxia-repressible gene sequences, proteins, or antibodies which specifically bind the proteins are disclosed. Methods for using the hypoxia-inducible and hypoxia-repressible gene sequences and proteins, and arrays thereof, to diagnose and treat hypoxia-related conditions such as cancer and ischemia are also provided.

L5 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:741942 CAPLUS
DOCUMENT NUMBER: 133:313708
TITLE: System for exsanguinous metabolic support of an organ or tissue
INVENTOR(S): Brasile, Lauren
PATENT ASSIGNEE(S): Breonics, Inc., USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061166	A1	20001019	WO 2000-US9894	20000413

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-129257 P 19990414
AB An exsanguinous metabolic support system (MSS) for maintaining an organ or tissue at a near normal metabolic rate is disclosed. The system employs a warm perfusion soln. capable of supporting the metab. of the organ or tissue thereby preserving its functional integrity. The system also monitors parameters of the circulating perfusion soln., such as pH, temp., osmolarity, flow rate, vascular pressure and partial pressure of respiratory gases, and regulates them to insure that the organ is maintained under near-physiol. conditions. Use of the system for long-term maintenance of organs for transplantation, for resuscitation and repair of organs having sustained warm ischemic ***damage*** , as a pharmaceutical delivery system and prognosticator of post transplantation organ function is also disclosed. Canine kidneys were isolated and renal artery was cannulated and the soln. was applied with the process and system of the present invention. The kidneys were maintained with the support of the MSS organ culture technol. at 32.degree. for 3 days. The kidneys remained intact and continued to metabolize during the period of organ culture. The ongoing metab. in the kidneys remained sufficient to result in continued function, i.e., the kidneys continued to produce urine throughout the period of the organ culture. There was no deterioration in

metab. or function in any parameter category during the period of MSS organ culture. Similarly, no edema developed nor was any necrosis obsd. following histol. evaluation.

REFERENCE COUNT: 13

REFERENCE(S):
(6) Flax; Med Biol Eng Comput 1979, V17(2), P199 CAPLUS
(9) Nakamura; Artificial Organs 1999, V23(2), P153 CAPLUS
(10) Roth; US 5747469 A 1998 CAPLUS
(11) The American National Red Cross; WO 9300808 A1 1993 CAPLUS
(12) Thurman; US 5484789 A 1996 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:144743 CAPLUS
DOCUMENT NUMBER: 132:203140
TITLE: Stable hypoxia-inducible factor-1.alpha. and method of use
INVENTOR(S): Semenza, Gregg L.
PATENT ASSIGNEE(S): The Johns Hopkins University School of Medicine, USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000010578	A1	20000302	WO 1999-US19416	19990825
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6124131	A	20000926	US 1998-148547	19980825
AU 9956914	A1	20000314	AU 1999-56914	19990825
EP 1107768	A1	20010620	EP 1999-943916	19990825
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001000920	A	20010423	NO 2001-920	20010223

PRIORITY APPLN. INFO.: US 1998-148547 A 19980825
WO 1999-US19416 W 19990825

AB Substantially purified stable human hypoxia-inducible factor-1.alpha. (HIF-1.alpha.) proteins and polynucleotides encoding them are useful for treating hypoxia- or ischemia-related tissue ***damage*** . The proteins are variant forms of HIF-1.alpha. that are stable under both hypoxic and nonhypoxic conditions, as well as chimeric proteins having HIF-1.alpha. DNA-binding and dimerization domains and a heterologous transactivation domain. The variants contain amino acid deletions or substitutions that substantially increase their half-life in cells under nonhypoxic conditions, such that the stable HIF-1.alpha. protein accumulates to much higher levels than wild-type HIF-1.alpha. under these conditions, and therefore mediates increased transcription of

hypoxia-inducible genes normally regulated by HIF-1.alpha., such as those for ***erythropoietin*** , vascular ***endothelial*** growth factor, heme oxygenase 1, NO synthase, and glycolytic enzymes. Depending on the activation domain utilized in the chimeric proteins, the transcriptional activity of stable HIF-1.alpha. may be regulated by O2 concn. or may be constitutive.

REFERENCE COUNT: 1
REFERENCE(S): (1) The Johns Hopkins University School of Medicine; WO 96/39426 A1 1996 CAPLUS

L5 ANSWER 6 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:312025 BIOSIS
DOCUMENT NUMBER: PREV200100312025
TITLE: Role of HIF-1alpha in proliferation and terminal differentiation of red cell progenitors.
AUTHOR(S): Divoky, Vladimir (1); Ciavatta, Dominic; Bailey, Evans; Townes, Tim M.; Semenza, Gregg; Prchal, Josef T.
CORPORATE SOURCE: (1) Olomouc Czech Republic
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 671a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

AB HIF-1 is a transcription factor that mediates oxygen homeostasis through oxygen availability. When oxygen tension is, HIF-1 initiates expression of several target genes; including genes encoding ***erythropoietin*** (EPO) and vascular ***endothelial*** growth factor (VEGF) which are known to regulate erythropoiesis and angiogenesis. Targeted disruption (knock-out, KO) of both HIF-1 subunits, alpha and beta, lead to embryonic lethality at embryonic day (ED) 10.5 due to multiple malformations. HIF-1alpha KO phenotype includes cardiovascular ***damage*** , abnormal cephalic vascularization and developmental arrest. In order to understand the role of HIF-1alpha in erythropoiesis, we studied yolk sac (YS) erythroid progenitors of HIF-1alpha KO homozygous (HIF-1alpha -/-), heterozygous (HIF-1alpha -/+) and wild-type (WT, HIF-alpha +/+) mouse embryos. At ED 9.5-10.0, dissected YS tissues were dissagregated and the cells were analyzed by in vitro hematopoietic colony assays. In comparison with WT littermates, the total number of YS cells was decreased by 50% in HIF-1alpha -/- embryos and was mildly decreased in HIF-1alpha -/+ embryos. The total number CFU-E and BFU-E/Mix erythroid colonies, when normalized per total number of YS cells, were reduced approximately 2-3 fold in HIF-1alpha -/- embryos and to a lesser degree in HIF-1alpha -/+ embryos. In addition, there was a marked difference in the proliferative capacity of the early myeloid progenitor cells. The sizes (cellularity) of the CSF/IL3/EPO-induced CFU-Mix colonies derived from the HIF-1alpha -/- embryos were 2-5 times smaller than the colonies derived from the WT embryos. This was due to a partial block of expansion and terminal differentiation of the erythroid component of HIF-1alpha-/- CFU-Mix colonies. Unlike the WT cells the HIF-1alpha defficient erythroid cells were not fully hemoglobinized. Neither EPO nor VEGF plus EPO added to the cultures fully rescued the defect in terminal differentiation of HIF-1alpha-/- erythroid cells. These results suggest that the HIF-alpha deficiency may lead to unidentified defects that may include deficinecies in regulatution of iron metabolism.

L5 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:795994 CAPLUS
DOCUMENT NUMBER: 132:31744
TITLE: Gene probes used for genetic profiling in healthcare screening and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Ltd., UK
SOURCE: PCT Int. Appl., 745 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964627	A2	19991216	WO 1999-GB1780	19990604

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
GB 1998-12099	A	19980606
GB 1998-13291	A	19980620
GB 1998-13611	A	19980624
GB 1998-13835	A	19980627
GB 1998-14110	A	19980701
GB 1998-14580	A	19980707
GB 1998-15438	A	19980716
GB 1998-15574	A	19980718
GB 1998-15576	A	19980718
GB 1998-16085	A	19980724
GB 1998-16086	A	19980724
GB 1998-16921	A	19980805
GB 1998-17097	A	19980807
GB 1998-17200	A	19980808
GB 1998-17632	A	19980814
GB 1998-17943	A	19980819

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their

sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic.RTM." profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

L5 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:795993 CAPLUS
DOCUMENT NUMBER: 132:31743
TITLE: Gene probes used for genetic profiling in healthcare screening and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Limited, UK
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964626	A2	19991216	WO 1999-GB1779	19990604
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9941586	A1	19991230	AU 1999-41586	19990604
AU 9941587	A1	19991230	AU 1999-41587	19990604
GB 2339200	A1	20000119	GB 1999-12914	19990604
EP 1084273	A1	20010321	EP 1999-925207	19990604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:

GB 1998-12098	A	19980606
GB 1998-28289	A	19981223
GB 1998-16086	A	19980724
GB 1998-16921	A	19980805
GB 1998-17097	A	19980807
GB 1998-17200	A	19980808
GB 1998-17632	A	19980814
GB 1998-17943	A	19980819
WO 1999-GB1779	W	19990604

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice

and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies.

L5 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:594848 CAPLUS
DOCUMENT NUMBER: 131:223977
TITLE: Compositions and methods for inducing neovascularization using a vascularization modulating agent such as GM-CSF
INVENTOR(S): Isner, Jeffrey M.; Asahara, Takayuki
PATENT ASSIGNEE(S): St. Elizabeth's Medical Center, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9945775	A1	19990916	WO 1999-US5130	19990309
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9930737	A1	19990927	AU 1999-30737	19990309
EP 1061800	A1	20001227	EP 1999-912344	19990309
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1998-77262 P 19980309
WO 1999-US5130 W 19990309

AB The present invention generally provides methods for modulating formation of new blood vessels. In one embodiment, the methods include administering to a mammal an effective amt. of a vascularization modulating agent (such as granulocyte macrophage-colony stimulating factor) sufficient to form the new blood vessels. Addnl. provided are methods for preventing or reducing the severity of blood vessel ***damage*** in a mammal which methods preferably include administering to the mammal an effective amt. of GM-CSF or another vascularization modulating agent. Instead of the proteins themselves being administered, the DNA encoding for the vascularization modulating agents can be administered. Addnl., the vascularization modulating agent can also be coadministered with at least one angiogenic protein. In addn. to administering the vascularization modulating agent to treat ischemic tissue, it's also possible to contact isolated ***endothelial*** progenitor cells (EPCs) with an amt. of an angiogenic protein sufficient

to induce proliferation of the EPCs and then administer the proliferated EPCs to treat the ischemic tissue. Provided also as part of this invention are pharmaceutical products and kits for inducing formation of new blood vessels in the mammal.

REFERENCE COUNT: 5

REFERENCE(S): (1) Hammond; US 5880090 A 1999 CAPLUS
(2) Leibovivh; US 4808402 A 1989 CAPLUS
(3) Saliba; US 4879282 A 1989 CAPLUS
(4) Sunderkotter; Pharmac Ther 1991, V51, P195 MEDLINE
(5) Takahashi; Nature Medicine 1999, V5(4), P434 CAPLUS

L5 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:377859 CAPLUS
DOCUMENT NUMBER: 131:28654
TITLE: Fusion proteins of transactivating transcription factors and their in expression of foreign genes in animal cells
INVENTOR(S): Gregory, Richard J.; Vincent, Karen
PATENT ASSIGNEE(S): Genzyme Corporation, USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9928469	A1	19990610	WO 1998-US25753	19981204
W: AU, CA, IL, JP, MX, NO, NZ, SG, US, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9916268	A1	19990616	AU 1999-16268	19981204
EP 1034267	A1	20000913	EP 1998-960741	19981204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NO 2000002849	A	20000802	NO 2000-2849	20000602

PRIORITY APPLN. INFO.: US 1997-67546 P 19971204
US 1998-133612 A 19980813
WO 1998-US25753 W 19981204

AB Genes for fusion proteins of transactivating transcription factors that use a DNA binding domain of a DNA binding protein and a protein domain capable of transcriptional activation are described for use in the expression of foreign genes in animal cells. Expression vectors for these genes are also described. Transgenic cell lines and animals expressing the genes are also described. In particular, hypoxia-inducible expression constructs that can be used in preventing ischemic ***damage*** assocd. with hypoxia-related disorders are provided. A constitutive transcription factor using the DNA binding domains of HIF-1.alpha. and the transactivation domain of VP16 is described. This form of the factor directed expression of a luciferase reporter gene from the promoters of the vascular ***endothelial*** growth factor (VEGF) or ***erythropoietin*** genes. The factor also increased expression of the VEGF gene in cell culture. A fusion protein of HIF-1.alpha. and NF-.kappa.B is also characterized.

REFERENCE COUNT: 10

REFERENCE(S): (1) Dachs, G; Nature Medicine 1997, V3(5), P515 CAPLUS
(2) Ema, M; Proc Natl Acad Sci 1997, V94, P4273 CAPLUS

09525808
(3) Jiang, B; J Biol Chem 1997, V272(31), P19253 CAPLUS
(4) Kirk, H; WO 9626742 A 1996 CAPLUS
(5) Li, H; J Biol Chem 1996, V271(35), P21262 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 24 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1999292316 MEDLINE
DOCUMENT NUMBER: 99292316 PubMed ID: 10366194
TITLE: A potential role for ***erythropoietin*** in focal permanent cerebral ischemia in mice.
AUTHOR: Bernaudin M; Marti H H; Roussel S; Divoux D; Nouvelot A; MacKenzie E T; Petit E
CORPORATE SOURCE: Universite de Caen, UMR 6551-CNRS, France.
SOURCE: JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM, (1999 Jun) 19 (6) 643-51.
Journal code: HNL; 8112566. ISSN: 0271-678X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990712
Last Updated on STN: 20000303
Entered Medline: 19990622
AB The present study describes, for the first time, a temporal and spatial cellular expression of ***erythropoietin*** (Epo) and Epo receptor (Epo-R) with the evolution of a cerebral infarct after focal permanent ischemia in mice. In addition to a basal expression of Epo in neurons and astrocytes, a postischemic Epo expression has been localized specifically to ***endothelial*** cells (1 day), microglia/macrophage-like cells (3 days), and reactive astrocytes (7 days after occlusion). Under these conditions, the Epo-R expression always precedes that of Epo for each cell type. These results support the hypothesis that there is a continuous formation of Epo, with its corresponding receptor, during the active evolution of a focal cerebral infarct and that the Epo/Epo-R system might be implicated in the processes of neuroprotection and restructuring (such as angiogenesis and gliosis) after ischemia. To support this hypothesis, a significant reduction in infarct volume (47%; $P < 0.0002$) was found in mice treated with recombinant Epo 24 hours before induction of cerebral ischemia. Based on the above, we propose that the Epo/Epo-R system is an endogenous mechanism that protects the brain against ***damages*** consequent to a reduction in blood flow, a mechanism that can be amplified by the intracerebroventricular application of exogenous recombinant Epo.

L5 ANSWER 12 OF 24 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1999318034 MEDLINE
DOCUMENT NUMBER: 99318034 PubMed ID: 10391150
TITLE: Picroliv -- a natural product protects cells and regulates the gene expression during hypoxia/reoxygenation.
AUTHOR: Gaddipati J P; Madhavan S; Sidhu G S; Singh A K; Seth P; Maheshwari R K
CORPORATE SOURCE: Center for Combat Casualty and Life Sustainment Research, Department of Pathology, Uniformed Services University of the Life Sciences, Bethesda, Maryland 20814, USA.
SOURCE: MOLECULAR AND CELLULAR BIOCHEMISTRY, (1999 Apr) 194 (1-2) 271-81.
Journal code: NGU; 0364456. ISSN: 0300-8177.
PUB. COUNTRY: Netherlands

09525808
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990816
Last Updated on STN: 19990816
Entered Medline: 19990803

AB Cellular adaptation to hypoxia involves regulation of specific genes such as vascular ***endothelial*** growth factor (VEGF), ***erythropoietin*** (EPO) and hypoxia inducible factor (HIF)-1 . In this study, we have evaluated the protective effect of picroliv (a purified iridoid glycoside fraction from roots of Picrorhiza kurrooa with hepatoprotective, anti-inflammatory and antioxidant properties) against hypoxic injury by examining lactate dehydrogenase (LDH) release in Hep 3B and Glioma cells. The expression of hypoxia regulated genes, VEGF and HIF-1 was studied in human umbilical vein ***endothelial*** cells (HUVEC), Hep 3B and Glioma cells. Picroliv reduced the cellular ***damage*** caused by hypoxia as revealed by a significant reduction in LDH release compared to untreated control. The expression of VEGF and HIF-1 subunits (HIF-1alpha and HIF-1beta) was enhanced by treatment with picroliv during normoxia and hypoxia in HUVEC and Hep 3B cells and on reoxygenation the expression of these genes was significantly reduced as revealed by mRNA analysis using RT-PCR. Simultaneous treatment with picroliv during hypoxia inhibited VEGF and HIF-1 expression in Glioma cells whereas the expression was not reduced by picroliv treatment during reoxygenation as evidenced by both RT-PCR and Northern hybridization. VEGF expression as revealed by immunofluorescence studies correlates well with the regulations observed in the mRNA expression. We have also examined the kinase activity of tyrosine phosphorylated proteins and protein kinase C (PKC) in Glioma cells treated with picroliv during hypoxia/reoxygenation. A selective inhibition of protein tyrosine kinase activity leading to tyrosine dephosphorylation of several proteins including 80 kd protein, and a reduction in PKC was seen in cells treated with picroliv and hypoxia. These findings suggest that picroliv may act as a protective agent against hypoxia/reoxygenation induced injuries, and the underlying mechanism may involve a novel signal transduction pathway.

L5 ANSWER 13 OF 24 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1999333169 MEDLINE
DOCUMENT NUMBER: 99333169 PubMed ID: 10406511
TITLE: Effects of recombinant human ***erythropoietin*** on functional and injury ***endothelial*** markers in peritoneal dialysis patients.
AUTHOR: Aguilera A; Selgas R; Ruiz-Caravaca M L; Bajo M A; Cuesta M V; Plaza M A; Hernanz A
CORPORATE SOURCE: Servicios de Nefrologia, Hematologia-Analitica y Bioquimica, Hospitales Universitarios de la Princesa y La Paz, Madrid, Spain.
SOURCE: PERITONEAL DIALYSIS INTERNATIONAL, (1999) 19 Suppl 2 S161-6.
Journal code: A2I; 8904033. ISSN: 0896-8608.
PUB. COUNTRY: Canada
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990910
Last Updated on STN: 19990910
Entered Medline: 19990824

AB Clinical effects of recombinant human ***erythropoietin*** (rHuEPO) such as thrombosis, convulsions, hyperviscosity, hypertension, and angiogenic effect in culture cells have been described. We studied the rHuEPO effect on ***endothelial*** ***damage*** markers and ***endothelial*** function markers: tissue-type plasminogen activator (t-PA), nitrate (NO3), thrombomodulin (TM), and von Willebrand factor (vWF). Twenty-six peritoneal dialysis patients treated with rHuEPO and 19 controls were included. The study design for rHuEPO patients consisted of four periods: long-term treatment (rHuEPO-1); 2 months of withdrawal (rHuEPO-2); and 4 months on 5000 IU/week rHuEPO subcutaneously, with markers being measured after 2 months (rHuEPO-3) and after 4 months (rHuEPO-4). After 2 months of rHuEPO withdrawal, a decrease in hemoglobin level appeared (11+/-1.8 g/dL to 9.2+/-1.5 g/dL, $p < 0.01$). After rHuEPO reintroduction, this value reached 10.6+/-1.5 g/dL at two months, and 11.1+/-1.4 g/dL at four months. A significant increase in t-PA ratio was observed from two months without rHuEPO to two months on rHuEPO, returning to previous values after four months. Similarly, TM increased for patients with creatinine clearances (CrC) < 5 mL/min. No changes in the higher-than-normal plasma vWF levels were found during the various periods. A statistically significant lower value was found in controls compared with rHuEPO-4 patients. A statistically significant increase in NO3 levels was observed in the pre-venous occlusion (VO) test immediately after the re-introduction of rHuEPO.This increment returned to prior values four months after rHuEPO was reintroduced. Our results show that rHuEPO treatment causes an increase in some ***endothelial*** ***damage*** markers (TM, t-PA) and modifies ***endothelial*** function markers (t-PA ratio, NO3). These changes might favor thrombosis and atherosclerosis.

L5 ANSWER 14 OF 24 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1999134397 EMBASE

TITLE: [Effect of ***erythropoietin*** in mitomycin-induced hemolytic-uremic syndrome].
RISPOSTA ALL' ERITROPOIETINA NELLA SINDROME EMOLITICO-UREMICA INDOTTA DA MITOMICINA.

AUTHOR: Catalano C.; Gianesini C.; Fabbian F.; Lambertini D.

CORPORATE SOURCE: Dr. C. Catalano, UO di Nefrologia e Dialisi, Via Marconi, 19, 35043 Monselice (PD), Italy. carletto.c@iol.it

SOURCE: Giornale Italiano di Nefrologia, (1999) 16/1 (21-24).
Refs: 13
ISSN: 0393-5590 CODEN: GINEEZ

COUNTRY: Italy

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer
025 Hematology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology

LANGUAGE: Italian

SUMMARY LANGUAGE: English; Italian

AB Background. Mitomycin C is a powerful antineoplastic agent used in the treatment of intestinal neoplasms. If used at high dosage, it may cause a secondary form of adult hemolytic-uremic syndrome (HUS). If this is the case, it has been suggested that blood transfusions may worsen the evolution of HUS. Heterologous blood may cause intravascular hemolysis causing ***endothelial*** ***damage*** and worsening of anemia, renal failure and thrombocytopenia. Methods and Results. We describe a clinical case in which a patient developed HUS after treatment with mitomycin C (150 mg/m2) for a carcinoma of the ascending colon. Repeated

blood transfusions were associated with rapidly evolving renal failure coupled with anemia and thrombocytopenia. Haptoglobin was undetectable. Soon after starting subcutaneous ***erythropoietin*** , we observed a stabilization of the renal failure whilst no more blood transfusions were required and haptoglobin levels returned to normal. Two years later, the patient's renal function slowly worsened but the patient is still totally asymptomatic. All investigations failed to show a relapse of her adenocarcinoma. Conclusions. We suggest that ***erythropoietin*** may be useful in mitomycin-induced HUS. A possible explanation is that ***erythropoietin*** allow interruption of blood transfusions, which may both trigger and perpetuate the syndrome. However, we cannot exclude a primary effect of ***erythropoietin*** on the endothelium or on the platelets.

L5 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:180734 CAPLUS
DOCUMENT NUMBER: 128:226687
TITLE: Method using ***erythropoietin*** for treating ***endothelial*** injury due to chemo- or radiotherapy, mechanical trauma, or disease
INVENTOR(S): Anagnostou, Athanasius A.; Sigounas, George
PATENT ASSIGNEE(S): East Carolina University, USA; Anagnostou, Athanasius A.; Sigounas, George
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9810650	A1	19980319	WO 1997-US15966	19970910
W: CA, CN, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5922674	A	19990713	US 1997-842700	19970415
EP 933995	A1	19990811	EP 1997-940974	19970910
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1235512	A	19991117	CN 1997-199338	19970910
JP 2001503028	T2	20010306	JP 1998-513794	19970910

PRIORITY APPLN. INFO.: US 1996-712358 A 19960911
WO 1997-US15966 W 19970910

AB The use of human ***erythropoietin*** (EPO) to prevent or treat ***endothelial*** injury due to chemotherapy, radiation therapy, mech. trauma, or to a disease state which ***damages*** the endothelium (such as inflammation, heart disease or cancer) is described. The use of EPO in conjunction with the administration of chemotherapeutic agents is described. The effects of ***erythropoietin*** on ***endothelial*** cells was detd. when administered before, after, or simultaneously with cisplatin.

L5 ANSWER 16 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:26358 BIOSIS
DOCUMENT NUMBER: PREV199900026358
TITLE: Effect of ***erythropoietin*** (EPO) on ***endothelial*** ***damage*** and function markers in peritoneal dialysis (PD) patients.
AUTHOR(S): Aguilera, A. (1); Ruiz-Caravaca, M. L.; Bajo, M. A.; Plaza,

09525808

M. A.; Hernanz, A.; Cuesta, M. V.; Selgas, R.
CORPORATE SOURCE: (1) Hosp. Univ. La Paz, Madrid Spain
SOURCE: Journal of the American Society of Nephrology, (Sept., 1998) Vol. 9, No. PROGRAM AND ABSTR. ISSUE, pp. 289A. Meeting Info.: 31st Annual Meeting of the American Society of Nephrology Philadelphia, Pennsylvania, USA October 25-28, 1998 American Society of Nephrology . ISSN: 1046-6673.
DOCUMENT TYPE: Conference
LANGUAGE: English

L5 ANSWER 17 OF 24 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1998092733 MEDLINE
DOCUMENT NUMBER: 98092733 PubMed ID: 9430862
TITLE: Altered flow-dependent vasodilatation of conduit arteries in maintenance haemodialysis.
AUTHOR: Joannides R; Bakkali E H; Le Roy F; Rivault O; Godin M; Moore N; Fillastre J P; Thuillez C
CORPORATE SOURCE: Department of Pharmacology, VACOMED, IFRMP 23, Rouen University Medical School, France.
SOURCE: NEPHROLOGY, DIALYSIS, TRANSPLANTATION, (1997 Dec) 12 (12) 2623-8.
Journal code: N7J; 8706402. ISSN: 0931-0509.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980226
Last Updated on STN: 19980226
Entered Medline: 19980219

AB BACKGROUND: An altered arterial nitric oxide (NO) pathway could partly explain the ***damage*** to arteries observed in haemodialyzed (HD) patients. The present study was designed to non-invasively evaluate the NO pathway of peripheral conduit arteries in HD patients. METHODS: Twelve normotensive, non-diabetic HD patients treated with ***erythropoietin*** and 12 matched healthy controls (C) were included in the study. The effect of endogenous release of NO was assessed by measuring the flow-dependent vasodilatation of the radial artery (post-ischaemic hyperaemia), and the response to exogenous NO assessed using sublingual glyceryl trinitrate administration (GTN). RESULTS: Radial artery diameter (echo-tracking), radial blood flow (RBF: Doppler) and mean arterial pressure (Finapres) were identical at baseline in HD patients and in healthy subjects. The flow-dependent vasodilatation of the radial artery was decreased in HD patients (C: 9 +/- 1% vs HD: 3 +/- 05%, P < 0.05). The decrease in radial vascular resistance (C: -44 +/- 4% vs HD: -24 +/- 2%, P < 0.05) and the increase in radial diameter (C: 31 +/- 2% vs HD: 25 +/- 2%, P < 0.05) after GTN administration were less in HD patients than in controls. The ratio between the increase in diameter after hyperaemia to the increase in diameter after GTN, was also diminished in HD patients (C: 30 +/- 3% vs HD: 13 +/- 2%, P < 0.001). CONCLUSIONS: The flow-dependent vasodilatation of peripheral conduit arteries is altered in HD patients and is associated with a slight but significant decrease in the vasodilating response to exogenous NO. These results suggest, in the absence of changes in basal radial vascular resistance and arterial diameter, more a decrease in ***endothelial*** NO bioavailability, than an increase in basal vascular tone.

L5 ANSWER 18 OF 24 MEDLINE DUPLICATE 5

09525808

ACCESSION NUMBER: 96327942 MEDLINE
DOCUMENT NUMBER: 96327942 PubMed ID: 8735172
TITLE: Evidence for amelioration of ***endothelial*** cell dysfunction by ***erythropoietin*** therapy in predialysis patients.
AUTHOR: Kuriyama S; Hopp L; Yoshida H; Hikita M; Tomonari H; Hashimoto T; Sakai O
CORPORATE SOURCE: Division of Nephrology, Saiseikai Central Hospital, Tokyo, Japan.
SOURCE: AMERICAN JOURNAL OF HYPERTENSION, (1996 May) 9 (5) 426-31. Journal code: AJI; 8803676. ISSN: 0895-7061.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961106
Last Updated on STN: 19961106
Entered Medline: 19961024

AB Evidence for the involvement of ***endothelial*** cells in the pathogenesis or ***erythropoietin*** -induced hypertension, and for ***endothelial*** cell ***damage*** in patients with chronic renal failure, has emerged and appears to be of major concern. We, therefore, investigated the effect of recombinant human ***erythropoietin*** (rHuEPO) therapy on endothelium-derived hormones in predialysis patients with progressive renal anemia. At the entry to the trial, the serum thrombomodulin concentration (Tm) and plasma endothelin-1 concentration (ET-1) in the predialysis patients were significantly higher than those in age- and sex-matched normal subjects. Following a 16 week period of treatment with 6000IU rHuEPO given intravenously once a week, patients' hematocrit increased from 27.1 +/- 2.6% to 34.6 +/- 3.2% (n = 16, P < .001). A positive correlation was found between Tm and serum creatinine concentration (Cr) (r = 0.61, P < .05 (n = 16), but no correlation was found between ET-1 and Cr. Tm and Tm/Cr significantly decreased from 7.9 +/- 2.8 ng/mL to 6.6 +/- 2.4 ng/mL (P < .01, n = 16), and from 2.1 +/- 0.7 (x10(-10) to 1.6 +/- 0.7 (x10(-10), P < .01, n = 16), respectively. However, there was no change in ET-1 as a result of the rHuEPO therapy. Creatinine clearance (Ccr), Cr, total amount of daily Tm excretion, Tm clearance/Ccr, daily urinary protein and albumin excretion, and blood pressure also remained unchanged throughout the trail. The present study indicates that correcting anemia by rHuEPO therapy reduces an abnormally elevated Tm in predialysis patients while blood pressure and renal function remain unchanged, suggesting that rHuEPO has a beneficial effect on ***endothelial*** cell dysfunction in chronic renal failure patients. This effect may be mediated via an improved oxygen supply to the ***endothelial*** cells due to the amelioration of anemia by rHuEPO.

L5 ANSWER 19 OF 24 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96215881 EMBASE
DOCUMENT NUMBER: 1996215881
TITLE: The molecular response of mammalian cells to hypoxia and the potential for exploitation in cancer therapy.
AUTHOR: Dachs G.U.; Stratford I.J.
CORPORATE SOURCE: Medical Research Council,Harwell, Didcot OX11 0RD, United Kingdom
SOURCE: British Journal of Cancer, (1996) 74/SUPPL. XXVII (S126-S132).
ISSN: 0007-0920 CODEN: BJCAAI

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 016 Cancer
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In this review, reports of the increased expression of selected genes in response to hypoxia have been summarised. The best studied mammalian hypoxia response systems are those of the ***erythropoietin*** (Epo) and the vascular ***endothelial*** growth factor (VEGF) genes, which will be described in some detail. Other genes discussed here include those encoding growth factors, cytokines, transcription factors, metabolic enzymes and DNA repair enzymes. Short DNA sequences (hypoxia response elements) governing the increased gene expression in response to hypoxia have been discovered in the vicinity of most of these genes. The review will end by analysing the possibility of exploiting tumour hypoxia via the use of hypoxia response elements for gene therapy of cancer.

L5 ANSWER 20 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1996:70294 BIOSIS
DOCUMENT NUMBER: PREV199698642429
TITLE: Endothelin-1 mediates ***erythropoietin*** -stimulated glomerular ***endothelial*** cell-dependent proliferation of mesangial cells.
AUTHOR(S): Nitta, Kosaku (1); Uchida, Keiko; Kimata, Naoki; Kawashima, Akira; Yumura, Wako; Nihei, Hiroshi
CORPORATE SOURCE: (1) Dep. Med., Kidney Center, Tokyo Women's Medical Coll., Tokyo 162 Japan
SOURCE: European Journal of Pharmacology Environmental Toxicology and Pharmacology Section, (1995) Vol. 293, No. 4-5, pp. 491-494.
ISSN: 0926-6917.
DOCUMENT TYPE: Article
LANGUAGE: English
AB These experiments were performed in an attempt to determine whether chronic stimulation of glomerular ***endothelial*** cells with recombinant human ***erythropoietin*** would alter mesangial cell proliferation. Glomerular ***endothelial*** cells in culture incubated with various concentrations of ***erythropoietin*** for up to 4 days exhibited dose-dependent endothelin-1 production. Moreover, the conditioned medium from ***erythropoietin*** -stimulated glomerular ***endothelial*** cells enhanced (3H)thymidine incorporation into mesangial cells. This enhancement was significantly attenuated in the presence of a endothelin A receptor antagonist, BQ-123. These results suggest that endothelin-1 mediates ***erythropoietin*** -stimulated glomerular ***endothelial*** cell-dependent mesangial cell proliferation, resulting in the progression of glomerulonephritis.

L5 ANSWER 21 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1996:236354 BIOSIS
DOCUMENT NUMBER: PREV199698800483
TITLE: Correction of PREVIEWS 98642429. Endothelin-1 mediates ***erythropoietin*** -stimulated glomerular ***endothelial*** cell-dependent proliferation of mesangial cells. Correction of volume number from 293 and correction of issue number from 4-5.
AUTHOR(S): Nitta, Kosaku (1); Uchida, Keiko; Kimata, Naoki; Kawashima, Akira; Yumura, Wako; Nihei, Hiroshi

09525808

CORPORATE SOURCE: (1) Dep. Med., Kidney Cent., Tokyo Women's Med. Coll., Tokyo 162 Japan
SOURCE: European Journal of Pharmacology Environmental Toxicology and Pharmacology Section, (1995) Vol. 5, No. 4, pp. 491-494.
ISSN: 0926-6917.
DOCUMENT TYPE: Article; Errata
LANGUAGE: English
AB These experiments were performed in an attempt to determine whether chronic stimulation of glomerular ***endothelial*** cells with recombinant human ***erythropoietin*** would alter mesangial cell proliferation. Glomerular ***endothelial*** cells in culture incubated with various concentrations of ***erythropoietin*** for up to 4 days exhibited dose-dependent endothelin-1 production. Moreover, the conditioned medium from ***erythropoietin*** -stimulated glomerular ***endothelial*** cells enhanced (3H)thymidine incorporation into mesangial cells. This enhancement was significantly attenuated in the presence of a endothelin A receptor antagonist, BQ-123. These results suggest that endothelin-1 mediates ***erythropoietin*** -stimulated glomerular ***endothelial*** cell-dependent mesangial cell proliferation, resulting in the progression of glomerulonephritis.

L5 ANSWER 22 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:316338 BIOSIS
DOCUMENT NUMBER: PREV199396024688
TITLE: Alterations in natural anticoagulant levels during allogeneic bone marrow transplantation: A prospective study in 27 patients.
AUTHOR(S): Leblond, V. (1); Salehian, B. D.; Borel, C.; Mapakou, C. P.; Dombret, H.; Sutton, L.; Binet, J-L.; Ankri, A.
CORPORATE SOURCE: (1) Dep. Hematology, Hopital Pitie-Salpetriere, 47 Boulevard de l'Hopital, Paris 75651 Cedex France
SOURCE: Bone Marrow Transplantation, (1993) Vol. 11, No. 4, pp. 299-305.
ISSN: 0268-3369.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The natural anticoagulants (antithrombin III, protein C, protein S), plasminogen and tissue plasminogen activator antigen (t-PA ag), were measured in 27 consecutive patients following allogeneic BMT. Thrombosis and veno-occlusive disease were not seen in this study. Changes in the levels of these proteins occurred mainly during acute GVHD. There were 14 patients who had no acute GVHD (group I) and 13 patients who had acute GVHD (group II). No changes in antithrombin III (ATIII), protein C, protein S and t-PA levels were found in group II before the appearance of acute GVHD when compared with group I. However, we noted a significant rise in protein S ($p = 0.01$), antithrombin III ($p = 0.001$) and t-PA ag ($p = 0.0004$) levels during acute GVHD. In contrast, protein C levels decreased early in GVHD ($p = 0.005$), and then increased progressively over the course of a month post-GVHD. No changes in plasminogen levels were observed. These results might reflect activation of and/or ***damage*** to ***endothelial*** cells during GVHD.

L5 ANSWER 23 OF 24 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92180531 EMBASE
DOCUMENT NUMBER: 1992180531
TITLE: ***Erythropoietin*** administration for renal anemia may increase coagulability and ***endothelial*** cell injury?.

09525808

AUTHOR: Akiba T.; Tachibana K.; Deguchi F.; Sakamoto N.; Ando R.; Sakurai S.; Chida Y.; Tomura N.; Yoshiyama N.; Hoshino M.; Marumo F.

CORPORATE SOURCE: Department of Internal Medicine, Tokyo Medical and Dental University, 1-5-45 Yushima,Bunkyoku, Tokyo 113, Japan

SOURCE: Japanese Journal of Artificial Organs, (1992) 21/3 (850-854).
ISSN: 0300-0818 CODEN: JNZKA7

COUNTRY: Japan

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 006 Internal Medicine
025 Hematology
028 Urology and Nephrology
037 Drug Literature Index

LANGUAGE: Japanese

SUMMARY LANGUAGE: English; Japanese

L5 ANSWER 24 OF 24 MEDLINE DUPLICATE 6

ACCESSION NUMBER: 93022339 MEDLINE

DOCUMENT NUMBER: 93022339 PubMed ID: 1405328

TITLE: Effect of dialyzer geometry during hemodialysis with cuprophane membranes.

AUTHOR: Taylor J E; McLaren M; Mactier R A; Henderson I S; Stewart W K; Belch J J

CORPORATE SOURCE: Renal Unit, Ninewells Hospital and Medical School, Dundee, Scotland, United Kingdom.

SOURCE: KIDNEY INTERNATIONAL, (1992 Aug) 42 (2) 442-7.
Journal code: KVB; 0323470. ISSN: 0085-2538.

PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199211

ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19990129
Entered Medline: 19921113

AB The effect of dialyzer geometry, both flat plate (FP) and hollow fiber (HF), on platelet and granulocyte activation during dialysis with cuprophane membranes was studied in 12 patients. A subset of six patients was restudied after correction of their anemia with recombinant human ***erythropoietin*** (EPO). Granulocyte count and aggregation in vitro fell significantly (P less than 0.01) at 20 minutes of dialysis, followed by a gradual return towards pre-dialysis values at 240 minutes. Malondialdehyde (MDA), a product of free radical reactions generated by activated granulocytes, increased significantly during dialysis [predialysis MDA (median, range): 8.4 (5.8 to 11.6) nmol/ml, 240 minutes MDA: 9.7 (6.6 to 12.5) nmol/ml, P less than 0.01 Wilcoxon test). This increase, however, was not affected by dialyzer geometry or EPO therapy. Neither type of dialyzer was associated with significant platelet loss at the end of dialysis. Whole blood platelet aggregation in vitro (spontaneous and collagen-induced) decreased significantly, (P less than 0.01) during dialysis, the fall in spontaneous aggregation being significantly less following EPO therapy [spontaneous aggregation 240 minutes; pre-EPO: 34 (13 to 52)%; post-EPO 50: (16 to 76)%, P less than 0.01)]. The ratio of the platelet release proteins beta-thromboglobulin and platelet factor 4 increased significantly during dialysis, indicating platelet activation in vivo, although there was no effect of dialyzer

geometry or EPO. Factor VIII von Willebrand Factor antigen, a putative marker of ***endothelial*** ***damage*** , was raised pre-dialysis, and increased further during dialysis, irrespective of dialyzer geometry or EPO. In conclusion, dialyzer geometry had no significant effect on granulocyte and platelet counts and activity during hemodialysis with cuprophane membranes.(ABSTRACT TRUNCATED AT 250 WORDS)

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(FILE 'HOME' ENTERED AT 17:52:15 ON 21 OCT 2001)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 17:52:26 ON 21 OCT 2001

L1	50703	S	ERYTHROPOIETIN
L2	0	S	(ENDOTHLELIAL CELL) AND DAMAGE?
L3	24240	S	ENDOTHELIAL AND DAMAGE?
L4	38	S	L1 AND L3
L5	24		DUP REM L4 (14 DUPLICATES REMOVED)